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SALVARSAN.

BY

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A CASE OF GRAVES' DISEASE WITH SCLERODERMA AND A POSITIVE WASSERMANN REACTION, TREAT- ED WITH SALVARSAN.*

By H. F. L. ZIEGEL, M.D.,

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Mrs. J. A., 28 years of age, has had no serious previous illness except malaria in Italy when she was 9 years old. Her menstruation started at 13. At the age of 15 she married. Her first child died of meningitis in infancy. Her second child, a boy 7 years of age, is healthy; in him the Wassermann was negative one year ago. Her husband gives no history or clinical evidence of syphilis; in him the Wassermann was negative in 1911. Four years ago she again became pregnant but aborted at the second month. Since then her menstruation has been regular, moderate, painless, of three days' duration, and without marked molimina.

The patient first came under my observation in August, 1911. She had been nervous since a child, but no swelling in the neck had been noticed till Dr. Howard Fox, who four months previously had seen her at the Skin and Cancer Hospital, called her attention to this swelling. For two years pre-

*Report read and case presented in the Section on Medicine, New York Academy of Medicine, May 20, 1913.

viously (so she said in August, 1911) she had been more nervous and there had also been cardiac palpitation on exertion, visual disturbance, and difficulty in swallowing. Five months previously a lump was noticed on the external aspect of the left arm just beneath the shoulder. Later other hard areas appeared on the arm, behind the shoulder, on the anterior aspect of the elbow, and on the upper forearm. There was no pain, but occasional slight pruritus. She slept and ate well and did not feel weak. Defecation and urination were normal. The patient came complaining of the annoyance due to the hardness and discoloration of the skin, which had been increasing rapidly, also of "nervousness," headaches, visual disturbance, difficulty in swallowing, and cardiac palpitation on exertion.

Physical examination made in August, 1911 (some of the negative findings being omitted), showed considerable uniform swelling of the thyroid gland, moderate exophthalmos, presence of Graefe's and Mœbius' signs, pulse frequency of 96° to 100°. No marked tremor. Extending from below the left cubital fossa upwards to the point of the shoulder, on the outer and front aspects of the left upper arm, and over the left scapula in the region of the spine, was a hardened condition of the skin, nodular in areas. The affected skin was discolored and furrowed, and in the central portions apparently longest involved it was slightly scaly. In some areas there was hard edema; here the skin could not be pinched up; it did not pit on pressure. Where most affected it was attached to the deeper tissues. The infiltration merged into the surrounding apparently normal skin. The color resembled somewhat that of ivory. There was no sclero-

dactylie, the skin of the lower forearm, hand, and fingers not being involved. The pupils reacted normally. Drs. Martin Cohen and Mulcahey made ophthalmoscopic examinations and found the fundus normal. There was slight general enlargement of the lymph nodes. The breasts were negative. The patient's weight was 149 pounds. The blood was negative as to anemia; the leucocytes numbered 9,000, with a slight relative increase of the mononuclear cells. The urine was negative.

August 18, 1911: the Noguchi modification of the Wassermann reaction performed at the Rockefeller Institute was positive. The Wassermann reaction performed by Dr. J. J. Hertz was positive. August 24: Salvarsan, 0.5 gram suspended in 3 c.c. of iodipin, was injected into the right sacrospinal muscle. On the following day the pain was slight at the site of injection, the pulse was 100, the rectal temperature was 100° F., and apparently no ill effects followed the treatment. August 29: Tumors of the skin softer. At the periphery of the areas where there is hard edema normal skin is replacing the hard patches. September 5: Further replacement by normal skin of sclerodermatous areas, especially those on the forearm and in the scapular region. Gaining in weight—now 150 pounds.

September 6, 1911: Repetition of salvarsan treatment; 0.5 gram of arsenobenzol in iodipin suspension injected into the left sacrospinal muscle. Though there was no constitutional reaction, the pain at the site of injection was very severe, and ever since then the patient has refused all injections. September 14: Further gain in weight, which is now 153½ pounds. The size of the thyroid gland has steadily diminished and the pulse

has continuously become less rapid since the first salvarsan injection. To-day the pulse frequency is 80. The second injection of salvarsan was not immediately followed by marked changes in the skin condition as was the first treatment. The urine is negative. Arsenous acid, 1/30 grain, and sajodin, 5 grains, were started t.i.d. October 19: Wassermann negative (Dr. Hertz). The luetin test performed ten days ago is negative. November 20: Slow but steady replacement of hard patches by normal skin. The patient says she is much less nervous than formerly. The pulse rate is now 76. The thyroid swelling has diminished markedly since the salvarsan treatment. December 18, 1911: Further improvement in the skin condition. As to the nodules beneath the spine of the scapula, many have gone entirely and the remaining ones are softer and more movable. The forearm and cubital fossa are now entirely free of the skin lesions. The patient no longer complains of headaches and is less nervous. Pulse 76. Weight 156 pounds.

The patient unfortunately refuses an intravenous injection of salvarsan, also another intramuscular injection, though further salvarsan treatment was strongly urged. February 12, 1912: There has been little change during the past two months in the skin condition; it is now about one-third of its extent when first seen a year and a half ago; the tumors beneath the skin are not nearly as numerous as originally and those that remain are softer. Weight 160¾ pounds. Pulse 72. May 6, 1912: Continuous improvement in the general condition. Weight now 164 pounds. Pulse 72. The patient has been getting Fowler's solution, 10 minims, t.i.d. December 20, 1912: During the past seven months there has been no marked increase nor diminution in

the extent of the morphea. Pulse 76. Arsenic internally continued, now in the form of the Dürckheimer Maxquelle water, 1 dram, t.i.d., p.c. April 1, 1913: There is noted some further improvement in the skin condition, which is now less than one-third of its extent when first seen by the writer. Bands of normal skin are extending into the affected areas, causing the latter to appear as islands. Most of the nodules disappeared after the salvarsan injections one year and a half ago, and those that remain are softer and smaller than originally. The patient absolutely refuses any more injections. The weight is now 179 pounds, *i.e.* a gain of 30 pounds since salvarsan was first given. The pulse frequency is 68. There is now very little swelling of the thyroid. Since the salvarsan treatment there has been no recurrence of the headaches, "nervousness," cardiac palpitation, and difficulty in swallowing. April 7, 1913: The luetin test has again been negative. Dr. Howard Fox and the New York Board of Health found the Wassermann negative.

Summary and Conclusions.—In a married woman 28 years of age with Graves' disease complicated with the circumscribed form of scleroderma or morphea the Wassermann reaction was positive. There was no history or clinical evidence of syphilis. In a son 7 years of age and in the husband the Wassermann was negative. Since two intramuscular injections of salvarsan of 0.5 gram each were given one year and nine months ago the Wassermann has been negative; moreover, the treatment with arsenobenzol was followed by a gain of 30 pounds in weight, by considerable diminution in the thyroid swelling, by disappearance of the nervous symptoms and the tachycardia, and by marked improvement in the skin condition. Most of the no-

dules in the skin disappeared, those that remain are softer and smaller, and the scleroderma is now less than one-third of its extent when first seen; the skin on the upper forearm, in the cubital fossa and the scapular region, which regions were originally involved, is now apparently normal. Unfortunately there was considerable pain caused by the second intramuscular injection, and ever since then further treatment with salvarsan has been refused, though an intravenous injection was advised; instead arsenic in various forms has been given by mouth.

From an experience limited to one case it would surely not be justifiable to draw conclusions as to the therapeutic value of salvarsan in the conditions described. Moreover, a rational interpretation of the changes that have taken place would have to be based partly upon answers to the following questions: Did this patient possibly have latent syphilis, despite the absence of anamnestic and clinical evidence of the disease, and were the favorable changes and the negative Wassermann due to the antiluetic effect of the salvarsan? Did the arsenic have a direct remedial influence on the Graves' disease and the scleroderma? Or did the improvement occur spontaneously and coincidentally, *after* rather than *because* of the arsenic therapy? Certain it is, however, that the administration of salvarsan and other forms of arsenic was followed by negative Wassermann reactions, by marked improvement in the scleroderma and by symptomatic cure of the Graves' disease.

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